UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,417	05/11/2001	Theo T. Nikiforov	01-054210US	7668

22798 7590 11/06/2002

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER
SIEW, JEFFREY

ART UNIT	PAPER NUMBER
1637	11

DATE MAILED: 11/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

file

Office Action Summary	Application No.	Applicant(s)	
	09/854,417	NIKIFOROV ET AL.	
	Examiner	Art Unit	
	Jeffrey Siew	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *39-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 9/21/01 is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7&8* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *notice to comply* .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 10 is acknowledged.

Claims 39-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II, there being no allowable generic or linking claim.

Election was made **without** traverse in Paper No. 10.

Specification

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

APPLICANT IS GIVEN THE RESPONSE PERIOD SET FORTH IN THIS OFFICE ACTION IN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136. In no case may an applicant extend the

period for response beyond the six month statutory period. Applicant is requested to return a copy of the attached Notice to Comply with the response.

2. In the Brief Description of Drawings, Figures 2,3 and 4 are not described properly. For example, Figure 2 is described in panels but the Drawings contains Figures 2A,2B…2E. Appropriate correction in the specification to reflect the actual figure nomenclature should be made.

Figure 7 has 3 panels but only Figure 7 is described in the specification.

Figure 10A and 10B are in the drawings but only Figure 10 is described in the specification.

On page 39 second to last paragraph is italicized.

On page 37 line 26, for example, a sequence of nucleotides requires sequence identifiers.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1,5-11,13-17,22, 23,25-27 & 36-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No.6,436,646 in view of Linn et al (US5,800,989 Sept, 1 1998). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 1,5-11,13-17,22, 23,25-27 & 36-38 are drawn to the method of hybridizing a first nucleic acid and second nucleic acid with a fluorescently labeled probe and detecting FP wherein the fluorescent label is neutral or positively charged.

Claims 1-12 of US 6,436,646 are drawn to the method of hybridizing a fluorescently labeled probe to target nucleic acid and detecting FP, monitoring and SNP detection. Claim 1 further drawn to adding polycation.

Claims 1-12 of US 6,436,646 are not drawn to neutral or positively charged fluorescent label.

Linn et al teach rhodamines which are neutral for FP detection of nucleic acid targets (see col. 9 line 49).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Linn et al's rhodamine dye to the method claims 1-12 of US 6,436,646 in order to provide for a label with an adequate fluorescent time for measuring. Linn et al teach a successful application of rhodamine dye to FP detection and the rhodamine dye provide optimal fluorescent lifetime for successful monitoring (see col. 9 lines 50-60). It would have been prima facie obvious to apply Linn et al's rhodamine dye to the method claims 1-12 of US,6,436,646 in order to provide a dye with an adequate fluorescence lifetime for successful detection.

Moreover, it is noted that claims 1-12 of US6,436,646 are drawn to the additional limitation of using a polycation which would represent a species of the generic method claims of the instant application which do not recite such a limitation (exc. claim 2).

4. Claims 1,2,5-11,13-17,22, 23,25-27,33 & 36-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8,9,10, 21-31 of U.S. Patent No.6,287,774 in view of Linn et al (US5,800,989 Sept, 1 1998). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 1,2,5-11,13-17,22, 23,25-27,33 & 36-38 are drawn to the method of hybridizing a first nucleic acid and second nucleic acid with a fluorescently labeled probe and detecting FP.

Claims 8,9,10,21-31 of US 6,436,646 are drawn to the method of hybridizing a fluorescently labeled probe to target nucleic acid and detecting FP, monitoring. Claim 8 is further drawn to polylysine.

Claims 8,9,10,21-31 of US 6,436,646 are not drawn to neutral or positively charged fluorescent label.

Linn et al teach rhodamines which are neutral for FP detection of nucleic acid targets (see col. 9 line 49).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Linn et al's rhodamine dye to the method claims 8,9,10,21-31 of US 6,436,646 in order to provide for a label with an adequate fluorescent time for measuring. Linn et al teach a successful application of rhodamine dye to FP detection and the rhodamine dye provide optimal fluorescent lifetime for successful monitoring (see col. 9 lines 50-60). It would

have been prima facie obvious to apply Linn et al's rhodamine dye to the method claims 9,10,21-31 of US 6,436,646 in order to provide a dye with an adequate fluorescence lifetime for successful detection.

5. Claims 1,5-11,13-17,22, 23,25-27 & 36-38 are directed to an invention not patentably distinct from claims 1-12 of commonly assigned US 6,436,646. Specifically, as recited above, claims 1,5-11,13-17,22, 23,25-27 & 36-38 would have been obvious over claims 1-12 of US 6,436,646 in view of Linn et al (US5,800,989).

5. Claims 1,2,5-11,13-17,22, 23,25-27,33 & 36-38 are directed to an invention not patentably distinct from 9,10, 21-31 commonly assigned of U.S. Patent No.6,287,774. Specifically, as recited above, claims 1,2,5-11,13-17,22, 23,25-27,33 & 36-38 would have been obvious over claims 9,10, 21-31 commonly assigned of U.S. Patent No.6,287,774 in view of Linn et al (US5,800,989).

7. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned US 6,287,774 and 6,436,646, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this

issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3,4,22, 23,34 & 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 22 & 23 recite detecting FP during hybridization but depend on claim 16 which recite hybridization occur before FP detection.

B) The term "polyion renders claims 3,4, 34 & 35 indefinite. It is unclear as to the scope of the term. It is unclear as to whether the term covers a multi charged ion such as Fe2+, or polycharged polymer etc.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,3-7,9,11, 14-17,22, 23,25, 34-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Linn et al (US5,641,633 June 24, 1997).

Linn et al teach a hybridization assay for detection by contacting a first nucleic acid with a second oligonucleotide probe with labeled rhodamine and detecting FP (see whole document esp.col. 8 lines 30-col. 9 line 45, col4 line s 50-53 & col.5 lines 3-10). They do not teach adding any polyion. They teach that larger molecules tumble slower than smaller molecules (see col.1 lines 19-26). The oligonucleotides may form double stranded form during hybridization (see col. 9 lines 40-42). They teach end point measurements of FP over real time starting at time 0 and after hybridization 9see col. 9 lines 55-60 & fig. 1). They perform measurements with signal

stranded oligonucleotide alone (see col. 10 line 62). They teach detection of target sequence from mycobacterium tuberculosis (see col. 14 line 44).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,2,5-11,13-27,33 & 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov (US.6,287,774 Sept. 11, 2001) in view of Linn et al (US5,800,989 Sept, 1 1998).

Nikiforov teaches a method of detecting by contacting a first nucleic acid to second nucleic acid with fluorescent label and detecting FP (see col.11 lines 8-17 & Figure 2). They teach the probe may be PNA (see col.11 line 22). They teach also the addition of polycation such as polylysine (see col.11 lines 49). They teach the detection of SNPs (see col. Example 4) with perfectly complementary probes and with targets with substituted base. They teach binding to both perfectly complementary and SNP target (see example 3). They teach plotting overtime and histogram (see Figure 15 & 16). Nikiforov teach rotational correctional time (see col.6).

Nikiforov do not explicitly teach neutral or positively charged fluorescent label.

Linn et al teach rhodamines which are neutral for FP detection of nucleic acid targets (see col. 9 line 49).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Linn et al's rhodamine dye to the Nikiforov method in order to provide for a label with an adequate fluorescent time for measuring. Linn et al teach a successful application of rhodamine dye to FP detection and the rhodamine dye provide optimal fluorescent lifetime for successful monitoring (see col. 9 lines 50-60). It would have been prima facie obvious to apply Linn et al's rhodamine dye to the Nikiforov's method in order to provide a dye with an adequate fluorescence lifetime for successful detection.

Moreover, Nikiforov et al teach that the FP rotational correlational time which would allow for real time detection during hybridization, it would have been prima facie obvious to monitor the binding over real time and plot the binding in histogram in order to examine the hybridization kinetics.

Moreover, as it was well known and practiced in the art to construct graphs and histograms to display data, it would have been prima facie obvious to characterize the data in histogram to differentiate the different data points.

11. Claims 12,13, 18-21,24 & 26-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Linn et al (US5,641,633 June 24, 1997) in view of Saiki et al (Nature vol. 324 Nov. 1986).

The teachings of Linn et al are described previously.

Linn et al do not teach testing multiple probes.

Saiki et al teach the use of allele specific oligonucletoides which when perfectly match hybridize and detecting mismatches and allelic variations in particular single base mutations (see whole doc. esp. abstract).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Saiki et al's teaching of allele specific probes to Linn et al's FP analysis method in order to detect allelic variation. It would have been prima facie obvious that apply Saiki et al's ASO probes with Linn et al's FP analysis in order to detect mutations including SNPs in real time with greater sensitivity.

Moreover, as it was well known and practiced in the art to construct graphs and histograms to display data, it would have been prima facie obvious to characterize the data in histogram to differentiate the different data points.

12. Claims 8,10 & 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Linn et al (US5,641,633 June 24, 1997) in view of Hyldig-Nielsen et al (US6,280,946 Aug. 28, 2001).

The teachings of Linn et al are described previously.

Linn et al do not teach PNAs.

Hyldig-Nielsen et al teach PNA probes for hybridization detection (see whole doc esp. abstract).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Hyldig-Nielsen et al's teaching of PNA probes to Linn et al's FP analysis in order to discriminate sequence variations. Hyldig-Nielsen et al teach the many advantages of

PNA probes including stability, long shelf life, independence of ionic strength, and greater efficiency in sequence determination (see col.1 lines 60-col.2 lines 5). It would have been prima facie obvious to apply PNA probes to Linn et al's FP analysis in order to increase the efficiency of sequence discrimination.

SUMMARY

13. No claims allowed.

CONCLUSION

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Monica Graves for Art Unit 1637 whose telephone number is (703)-306-2938.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and Before Final FAX (703) 872-9306 or After Final FAX (703) 30872-9307.

JEFFREY SIEW
PRIMARY EXAMINER

November 4, 2002

Application No.: 09/054417

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY